

NATIONAL VACCINE ADVISORY COMMITTEE

Report of the Subcommittee on Opportunities to Prevent Infectious Diseases by Developing New Vaccines (Dr. Small)

Approved By The Full Committee

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INTRODUCTION

This report lists diseases for which the development of new vaccines is considered possible. It proposes criteria to assign priorities to vaccine candidates and selects a limited number of diseases viewed by the Committee to be particularly important for vaccine development. Research on technologies that potentially cut across a disease oriented listing is also identified and considered equally important.

I. DISEASES THAT ARE POTENTIALLY PREVENTABLE BY NEW VACCINES-- Classified for prioritization by patient populations and by feasibility (as shown in Table 1)

A number of variables influence priorities for development of new vaccines. These include the urgency of the problem (whether epidemic or stable), the disease impact (morbidity and mortality), the vulnerability of patient populations, and the feasibility of producing and delivering a safe and effective vaccine.

In developing a priority list of new vaccine candidates, all of these variables compete. Table 1 presents diseases potentially preventable by new vaccine development, stratified by age of the target population and some of these other variables. Lists of priorities will be developed with some variation depending upon opportunities presented by new scientific knowledge and by discovery of new methodologies. Hard choices need to be made according to competing criteria, e.g., infant meningitis and pneumonia versus adolescent sexually transmitted diseases.

Despite the large number of variables, a consensus is necessary to help address the problem and allocate resources.

TABLE 1 DOMESTIC OPPORTUNITIES+

	VACCINE STATUS			
	Available vaccines which could be improved	Vaccines which could be available within five years	Vaccines of great importance needing concerted effort if they are to be available within ten years	More basic research required to determine feasibility
Infants/ Children	Pertussis H-flu B++ Pneumococcus++ Meningococcus++ Tetanus/Diph Measles	RSV Parainfluenza Rotavirus Hepatitis A CMV M.pneumoniae Varicella	HIV Herpes 1&2 EBV Shigella Salmonella E. coli	TB Hepatitis C Papilloma Lyme Parvovirus
Adolescents		Varicella	STDs HIV Herpes 1&2 Gonorrhea Chlamydia Treponema H ducreyi	
Adults	Influenza Pneumococcus	CMV Group B Strep* Hepatitis A Varicella	HIV Shigella Salmonella E. coli	

- + Many vaccines apply to more than one age group, but most are listed under the primary age group
- ++ conjugated vaccine candidates
- * immunization of pregnant women or females prior to childbearing age designed to protect children

II. NEW VACCINES FOR DISEASES OF GLOBAL RATHER THAN DOMESTIC SIGNIFICANCE

Respiratory and diarrheal diseases are particularly severe problems in developing countries. Several of these diseases, potentially preventable by new vaccines, cause substantial mortality in the developing world. Their control by vaccines would be of help in reducing infant mortality. Vaccines for other diseases protect travelers to affected regions and, in the case of several diseases, would protect the United States from importations. A leadership role in development and production strategies for new vaccines for these diseases should be a part of the National Vaccine Plan.

A. For infants and children (in addition to those listed in Table I)

Improved vaccines are needed for measles and polio because present vaccines have not proved adequate in many developing countries. Improved vaccines will also increase the likelihood of eradication of measles and polio. New vaccines for respiratory diseases would significantly reduce mortality and morbidity. Vectored vaccines or sustained release vaccines could greatly reduce the cost of immunization.

B. For all age groups: (in addition to those listed in Table 1)

Malaria heads the list in the urgency and magnitude of the problem. Accelerated development of several candidate vaccines is needed; however, because of the complexity of the disease, long term efforts may be required before a satisfactory vaccine is developed. Hence, malaria is listed in two columns in Table 2.

Dengue candidate vaccines can be targeted for accelerated development.

Enteric bacterial diseases such as cholera, shigella, salmonella and enteropathic E. coli need accelerated development of vaccines for the developing countries more urgently than for the United States.

Table 2 GLOBAL OPPORTUNITIES (IN ADDITION TO TABLE 1)

Vaccine status

GROUP

Available
vaccines
which
could be
improved

Vaccines
which could
be available
within
five years

Vaccines
of great
importance
needing
concerted
effort if
they are to
be available
within ten years

More basic
research
required
to determine
feasibility

Children

Measles
Polio
Diphtheria+
Tetanus+*
Pertussis+

Group A Strep
(Rheumatic Fever)

All ages

Japanese
Encephalitis
Rabies

Dengue
Enteric Bact. Infect.
(e.g., Cholera,
Shigella, Salmonella,
E.coli
Hemorrhagic
Fever Renal
Syndrome (Hantan)
Virus)

HIV
Malaria
Schistosomiasis

Malaria
TB
Leprosy

* immunization of pregnant women or females prior to childbearing age
designed to protect children

+ potential candidates for vectored vaccines and/or sustained release
preparations

III. METHODOLOGIC OPTIONS

In addition to the development of specific vaccines, there is a need for the development of new technologies to be applied to many different vaccines to increase efficacy, reduce adverse reactions, and/or reduce cost. These include:

1. Vectored vaccines

Active research is required to determine:

- a) which vectors are potentially usable in man?
- b) which genes can be introduced into which vectors to produce immunity?
- c) the maximum number of genes, identified in b), that can be inserted into a vector or mixture of vectors to produce the desired multivalent immune response?
- d) the desirability of incorporating genes coding for growth factors (lymphokines like IL-2) specific for immune system cells?

2. Adjuvants/delayed release vehicles

These approaches offer the potential to reduce the frequency of administration and perhaps the adverse reactions.

3. Synthetics

Synthetic peptides and conjugated vaccines offer approaches not available in past decades. They need to be actively explored.

4. Mucosal Immunity

Immunization procedures that stimulate production of local antibody and cell mediated immunity will be important for prevention of infection of mucosal surfaces, perhaps including sexually transmitted diseases.

5. Other Options

Other approaches including, for example, the use of virosomes, anti-idiotypic immunogens and/or cytokines could prove efficacious.

IV. RECOMMENDATIONS

A. The Committee believes that new vaccine development should be a high priority for the United States and the World. New vaccine candidates should be selected in accordance with the following criteria:

1. disease impact on specified patient populations
2. urgency
3. feasibility of producing and delivering safe and effective vaccines

B. The Committee recommends that the following new technologies be emphasized:

1. Vectored Vaccines

The advent of biotechnology has made it theoretically possible to insert the nucleic acid coding for appropriate antigens of a multitude of pathogens into a single viral or bacterial live vector. This would create a multivalent vaccine that might require only one administration to provide prolonged immunity.

2. Adjuvants and Delivery Systems

The potential savings offered by being able to reduce the frequency of vaccine administration warrant very active investigations in this area.

C. The Committee believes that among the opportunities for the improvements of existing vaccines and development of new vaccines, vaccines for the following diseases or disease groups should be pursued vigorously:

1. All Ages

HIV infection affects all age groups and is spreading. An important national priority is the development of a safe and effective vaccine. The mandate to accomplish this critical task falls outside the charge of the National Vaccine Program.

2. Children

- o New vaccines for pertussis are needed. This issue is discussed more fully in the report of the subcommittee on existing vaccines.
- o Vaccines for infant acute viral respiratory infections (RSV and parainfluenza) are urgently needed. Such vaccines could reduce morbidity and mortality for millions of U.S. infants each year, not to mention the rest of the world.
- o Vaccines for enteric infections are needed for all but especially for infants in developing nations. Vaccines for rotavirus, salmonella, shigella, and E.coli are feasible and could significantly reduce morbidity and infant mortality from these diseases.
- o Vaccines against invasive bacterial infection of children (H.influenza, b.strep. pneumoniae and N.meningitides) could reduce infant mortality and morbidity for hundreds of thousands of infants each year worldwide, if conjugated polysaccharide vaccines were available for administration to young infants. Group B Strep vaccines for pregnant women and/or women of childbearing age could prevent morbidity and mortality due to invasive bacterial disease of newborns.

3. Adolescents

Now perhaps more than ever before effective vaccines are needed to prevent sexually transmitted diseases (syphilis, herpes, gonorrhea, chlamydia and chancroid). Not only are STDs causing increasing morbidity in adolescents and young adults, but they are also important in enhancing the transmission of HIV. STDs are also a major cause of infertility. Feasibility of developing effective vaccines varies with the specific disease and is currently lower than with some of the other diseases listed above, but this makes the need to pursue development of STD vaccines all the more urgent.

4. Adults

The most urgent need for adults is an improved influenza vaccine. Influenza/pneumonia are the fourth leading cause of death in the elderly. There are existing vaccines for both, but they are under utilized, and the influenza vaccine is less than optimally effective. Development of improved vaccines would enhance both efficacy and delivery.

There are many other worthwhile vaccines to be developed, but, in view of the Committee, those listed above are most promising at this time.

V. SOME OF THE ISSUES REMAINING TO BE CONSIDERED

It will be necessary to also develop quantitative estimates of the following issues in relation of each of the recommendations:

1. Estimated time required to bring an effective vaccine to market
2. Cost of development
3. Potential savings